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(54) Title: **GTP-BINDING PROTEIN ASSOCIATED FACTORS**

(57) Abstract: The invention provides human GTP-binding associated proteins (GBAP) and polynucleotides which identify and encode GBAP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of GBAP.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/19698

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 G01N33/53 C12Q1/68 A61K38/17
C07K16/18 A01K67/027

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N C12Q A61K A01K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| X | <p>DATABASE EMBEST HUM1 [Online] Entry/Acc.no. AA679577, 4 December 1997 (1997-12-04) HILLIER, L. ET AL.: "zj49c09.s1 Soares fetal liver spleen INFLS S1 Homo sapiens cDNA clone 453616 3' similar to TR:G1230663 G1230663 SIMILAR TO E. COLI HYPOTHETICAL 22.1 KD PROTEIN IN POLA 3' REGION." XP002148938 the whole document</p> <p>---</p> <p>-/--</p> | 11-15 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

Internal Application No

PCT/US 00/19698

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|---|-----------------------------|
| X | DATABASE EMBL - EMBL HUM13 [Online] Entry HS1229641, Acc.no. AA429983, 25 May 1997 (1997-05-25) HILLIER, L. ET AL.: "zw60f01.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA cTone IMAGE:774457 5' similar to SW:YSXC BACSU P38424 HYPOTHETICAL 22.0 KD PROTEIN IN LON-HEMA INTERGENIC REGION ;, mRNA sequence." XP002148939 the whole document | 11-15 |
| A | --- DATABASE EMBL - EMBL ROD2 [Online] Entry/Acc.no. A1122094, 8 September 1998 (1998-09-08) MARRA, M. ET AL.: "uc46f10.r1 Soares mouse mammary gland NMLMG Mus musculus cDNA clone IMAGE:1401067 5' similar to SW:Y335 MYCGE P47577 HYPOTHETICAL GTP-BINDING PROTEIN MG335. ;, mRNA sequence." XP002148940 the whole document | |
| P,X | --- DATABASE EMBL - EMHUM2 [Online] Entry/Acc.no. AF161484, 1 February 2000 (2000-02-01) YE, M. ET AL.: "Homo sapiens HSPC135 mRNA, complete cds." XP002148941 the whole document | 1,3,6-9, 11-16, 20,23 |
| P,X | --- WO 99 58675 A (CHIRON CORP ;HYSEQ INC (US)) 18 November 1999 (1999-11-18) the whole document | 11-15 |
| A | --- CLAPHAM, D.E. ET AL.: "New roles for G-protein beta-gamma-dimers in transmembrane signalling." NATURE, vol. 365, 30 September 1993 (1993-09-30), pages 403-6, XP002148967 cited in the application the whole document ----- | |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/19698

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 18, 21 and 24 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-28 all partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1-28, all partially

A protein with at least 90% identity to seq.ID.1 or biologically active or immunogenic fragment thereof, polynucleotide encoding it, optionally transcriptionally linked to a promoter, cell transformed therewith, transgenic organism comprising said polynucleotide, method for producing said protein using said cell, antibody against said protein, polynucleotides having at least 70% sequence homology to seq.ID.67 of at least 60 nt, method for detecting said nucleic acid by hybridization with a probe of at least 20 nt or by amplification, pharmaceutical composition of the protein, methods for screening for (ant)agonists of the protein or modulators of the proteins expression or activity and compounds identified thereby.

Inventions 2-61: claims 1-28, all partially

Subject matter as defined above under invention 1, but limited to the respective protein/nucleic acid sequences:

2. 2 and 68,
3. 3 and 69,
4. 4 and 70,
5. 5 and 71,
6. 6 and 72,
7. 7 and 73,
8. 8 and 74,
9. 9 and 75,
- 10.10 and 76,
- 11.11 and 77,
- 12.12 and 78,
- 13.13 and 79,
- 14.14 and 80,
- 15.15 and 81,
- 16.16 and 82,
- 17.17 and 83,
- 18.18 and 84,
- 19.19 and 85,
- 20.20 and 86,
- 21.21 and 87,
- 22.22 and 88,
- 23.24 and 90,
- 24.25 and 91,
- 25.26 and 92,
- 26.27 and 93,
- 27.29 and 95,
- 28.30 and 96,
- 29.31 and 97,
- 30.32 and 98,
- 31.33 and 99,
- 32.34 and 100,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

33.36 and 102,
34.37 and 103,
35.38 and 104,
36.39 and 105,
37.40 and 106,
38.41 and 107,
39.43 and 109,
40.44 and 110,
41.45 and 111,
42.46 and 112,
43.47 and 113,
44.48 and 114,
45.49 and 115,
46.50 and 116,
47.52 and 118,
48.53 and 119,
49.54 and 120,
50.55 and 121,
51.56 and 122,
52.57 and 123,
53.58 and 124,
54.59 and 125,
55.60 and 126,
56.61 and 127,
57.62 and 128,
58.63 and 129,
59.64 and 130,
60.65 and 131, and
61.66 and 132.

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claim 12 of the underlying application relates to a polynucleotide comprising at least 60 nt of a polynucleotide, which has at least 70% sequence identity to a nucleic acid sequence selected from those listed in claim 5. Since the at least 60 nucleotides need not originate from an area of homology with any of the sequences of claim 5, the polynucleotide claimed in claim 12 is not defined in any way. The search of said claim has been limited to nucleic acids comprising a nucleic acid sequence having at least 70% homology to a nucleic acid sequence selected from claim 5 of at least 60 nt in length.

Present claims 20 and 23 refer to agonists and antagonists, respectively, defined by reference to a desirable characteristic or property, namely the fact that they can be obtained by certain screening methods. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to proteins with at least 90% homology to seq.ID.1 and antibodies thereto.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/19698

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|----------------------------|---------------------|
| WO 9958675 A | 18-11-1999 | AU 4187499 A | 29-11-1999 |
| | | AU 2095599 A | 19-07-1999 |
| | | EP 1053319 A | 22-11-2000 |
| | | WO 9933982 A | 08-07-1999 |
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| | | AU 6263999 A | 17-04-2000 |
| | | WO 0018916 A | 06-04-2000 |
| ----- | | | |